

WHAT IS CLAIMED IS:

- 1           1. An anti-mesothelin antibody which binds to recombinant mesothelin  
2 with a dissociation constant of less than  $3 \times 10^{-8}$  M and specifically binds to cells expressing  
3 mesothelin on their cell surface.
- 1           2. The antibody of claim 1, wherein the CDRs of said antibody are as  
2 indicated in SEQ ID NO:5.
- 1           3. The antibody of claim 1, comprising a single chain Fv antibody  
2 comprising a variable heavy ( $V_H$ ) region and a variable light ( $V_L$ ) region.
- 1           4. The antibody of claim 3, wherein said  $V_L$  is conjugated to said  $V_H$   
2 through a linker peptide.
- 1           5. The antibody of claim 3, wherein said antibody is a dsFv.
- 1           6. The antibody of claim 3, wherein the variable heavy ( $V_H$ ) region is  
2 encoded by SEQ ID NO:1.
- 1           7. The antibody of claim 3, wherein the variable light ( $V_L$ ) region is  
2 encoded by SEQ ID NO:1.
- 1           8. The antibody of claim 3, wherein said single chain Fv antibody  
2 comprises a variable heavy ( $V_H$ ) region and a variable light ( $V_L$ ) region encoded by SEQ ID  
3 NO:1.
- 1           9. The antibody of claim 1, wherein said antibody is detectably labeled.
- 1           10. The antibody of claim 1, wherein said antibody is conjugated to an  
2 therapeutic agent.

1                   11. The antibody of claim 10, wherein said therapeutic agent is a toxin.

1                   12. The antibody of claim 11, wherein said toxin is a *Pseudomonas*  
2                   exotoxin (PE) or cytotoxic fragment thereof.

1                   13. An anti-mesothelin antibody wherein the variable heavy (V<sub>H</sub>) region is  
2                   as shown in SEQ ID NO:5.

1                   14. An anti-mesothelin antibody wherein the variable light (V<sub>L</sub>) region is  
2                   as shown in SEQ ID NO:5.

1                   15. An anti-mesothelin antibody wherein the CDRs are as shown in SEQ  
2                   ID NO:5.

1                   16. An anti-mesothelin antibody wherein said antibody comprises a  
2                   variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID NO:5.

1                   17. The antibody of claim 16, wherein said antibody is a scFv.

1                   18. An anti-mesothelin antibody, said antibody produced by a process  
2                   comprising of the steps:

3                   (i) immunizing a mammal with an expression cassette which  
4                   comprises cDNA encoding mammalian mesothelin;

5                   (ii) removing the spleen from said mammal;

6                   (iii) preparing a phage display library from said spleen of said  
7                   animal;

8                   (iv) selecting for a phage which displays an antibody which binds to  
9                   recombinant mesothelin with a dissociation constant of less than 3 x 10<sup>-8</sup> M and specifically  
10                  binds to cells expressing mesothelin on their cell surface;

- (v) isolating the nucleic acid sequence which encodes said antibody;
- (vi) introducing said nucleic acid sequence into a cell such that said antibody is expressed by said cell; and
- (vii) isolating said antibody from said cell.

19. The antibody of claim 18, further comprising recombinantly fusing in frame said nucleic acid sequence with a nucleic acid sequence which encodes a *Pseudomonas* exotoxin or cytotoxic fragment thereof.

20. A recombinant immunoconjugate, comprising a therapeutic agent or a detectable label bonded to an anti-mesothelin antibody which binds to recombinant mesothelin with a dissociation constant of less than  $3 \times 10^{-8}$  M and specifically binds to cells expressing mesothelin on their cell surface.

21. The immunoconjugate of claim 20, wherein CDRs of said antibody are as indicated in SEQ ID NO:5.

22. The immunoconjugate of claim 20, comprising a single chain Fv antibody comprising a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region.

23. The immunoconjugate of claim 22, wherein said  $V_H$  region is peptide bonded to said  $V_L$  region through a linker peptide.

24. The immunoconjugate of claim 22, wherein the variable heavy (V<sub>H</sub>) region is encoded by SEQ ID NO:1.

25. The immunoconjugate of claim 22, wherein the variable light (V<sub>L</sub>) region is encoded by SEQ ID NO:1.

1           26. The immunoconjugate of claim 22, wherein said single chain Fv  
2 antibody comprises a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID  
3 NO:1.

1           27. The immunoconjugate of claim 20, wherein said antibody is  
2 conjugated to a therapeutic agent.

1           28. The immunoconjugate of claim 27, wherein said therapeutic agent is a  
2 toxin.

1           29. The immunoconjugate of claim 28, wherein said toxin is a  
2 *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1           30. The immunoconjugate of claim 29, wherein said cytotoxic fragment is  
2 PE38.

1           31. The immunoconjugate of claim 20, wherein said variable heavy (V<sub>H</sub>)  
2 region is peptide bonded to the therapeutic agent or detectable label.

1           32. The immunoconjugate of claim 20, wherein said immunoconjugate is  
2 encoded by SEQ ID NO:2.

1           33. An expression cassette encoding said antibody of claim 3.

1           34. The expression cassette of claim 33, wherein the CDRs of said  
2 antibody are as indicated in SEQ ID NO:5.

1           35. The expression cassette of claim 33, comprising a single chain Fv  
2 antibody comprising a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region.

1           36. The expression cassette of claim 35, wherein  $V_H$  region is peptide  
2 bonded to said  $V_L$  region through a linker peptide.

1           37. The expression cassette of claim 35, wherein the variable heavy ( $V_H$ )  
2 region is encoded by SEQ ID NO:1.

1           38. The expression cassette of claim 35, wherein the variable light ( $V_L$ )  
2 region is encoded by SEQ ID NO:1.

1           39. The expression cassette of claim 35, wherein said single chain Fv  
2 antibody comprises a variable heavy ( $V_H$ ) region and a variable light ( $V_L$ ) region of SEQ ID  
3 NO:1.

1           40. The expression cassette of claim 33, wherein said antibody is  
2 detectably labeled.

1           41. The expression cassette of claim 33, wherein said antibody is  
2 conjugated to a therapeutic agent.

1           42. The expression cassette of claim 41, wherein said therapeutic agent is a  
2 toxin.

1           43. The expression cassette of claim 42, wherein said toxin is a  
2 *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1           44. An expression cassette encoding said recombinant immunoconjugate  
2 of claim 22.

1           45. The expression cassette of claim 44, wherein CDRs of said antibody  
2 are as indicated in SEQ ID NO:5.

1           46. The expression cassette of claim 44, wherein said antibody is a single  
2 chain antibody comprising of a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region.

1           47. The expression cassette of claim 46, wherein said V<sub>H</sub> region is peptide  
2 bonded to said V<sub>L</sub> region through a linker peptide.

1           48. The expression cassette of claim 46, wherein the variable heavy (V<sub>H</sub>)  
2 region is encoded by SEQ ID NO:1.

1           49. The expression cassette of claim 46, wherein the variable light (V<sub>L</sub>)  
2 region is encoded by SEQ ID NO:1.

1           50. The expression cassette of claim 46, wherein said single chain antibody  
2 comprises a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID NO:1.

1           51. The expression cassette of claim 44, wherein said therapeutic agent is a  
2 toxin.

1           52. The expression cassette of claim 51, wherein said toxin is a  
2 *Pseudomonas* exotoxin (PE) or a cytotoxic fragment thereof.

1           53. The expression cassette of claim 52, wherein said cytotoxic fragment is  
2 PE38.

1           54. The expression cassette of claim 52, wherein a variable heavy region is  
2 peptide bonded to the *Pseudomonas* exotoxin (PE) or cytotoxic fragment thereof.

1           55. A host cell comprising said expression cassette of claim 33.

1           56. The host cell of claim 55, wherein the CDRs of said antibody are as  
2 indicated in SEQ ID NO:5.

1           57. The host cell of claim 55, comprising a single chain Fv antibody  
2 comprising a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region.

1           58. The host cell of claim 57, wherein said V<sub>H</sub> region is peptide bonded to  
2 said V<sub>L</sub> region through a linker peptide.

1           59. The host cell of claim 57, wherein the variable heavy (V<sub>H</sub>) region is  
2 encoded by SEQ ID NO:1.

1           60. The host cell of claim 57, wherein the variable light (V<sub>L</sub>) region is  
2 encoded by SEQ ID NO:1.

1           61. The host cell of claim 57, wherein said single chain Fv antibody  
2 comprises a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID NO:1.

1           62. The host cell of claim 55, wherein said antibody is detectably labeled.

1           63. The host cell of claim 55, wherein said antibody is conjugated to a  
2 therapeutic agent.

1           64. The host cell of claim 63, wherein said therapeutic agent is a toxin.

1           65. The host cell of claim 64, wherein said toxin is a *Pseudomonas*  
2 exotoxin (PE) or cytotoxic fragment thereof.

1           66. A host cell comprising said expression cassette of claim 44.

1           67. The host cell of claim 66, wherein CDRs of said antibody are as  
2 indicated in SEQ ID NO:5.

1           68. The host cell of claim 66, wherein said antibody is a single chain  
2 antibody comprising of a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region.

1           69. The host cell of claim 57, wherein said V<sub>H</sub> region is peptide bonded to  
2 said V<sub>L</sub> region through a linker peptide.

1           70. The host cell of claim 57, wherein the variable heavy (V<sub>H</sub>) region is  
2 encoded by SEQ ID NO:1.

1           71. The host cell of claim 57, wherein the variable light (V<sub>L</sub>) region is  
2 encoded by SEQ ID NO:1.

1           72. The host cell of claim 57, wherein said single chain antibody  
2 comprises a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID NO:1.

1           73. The host cell of claim 63, wherein said therapeutic agent is a toxin.  
1           74. The host cell of claim 73, wherein said toxin is a *Pseudomonas*  
2 exotoxin (PE) or a cytotoxic fragment thereof.

1           75. The host cell of claim 74, wherein said PE is PE38.  
1           76. A method for inhibiting the growth of a malignant cell expressing  
2 mesothelin on its cell surface, said method comprising:  
3           contacting said malignant mesothelial cell with an effective amount of an  
4 immunoconjugate comprising a toxin peptide bonded to an anti-mesothelin antibody which  
5 binds to recombinant mesothelin with a dissociation constant of less than 3 x 10<sup>-8</sup> M and  
6 specifically binds to cells expressing mesothelin on their cell surface.

1           77. The method of claim 76, wherein said antibody comprises CDRs as  
2 indicated in SEQ ID NO:5.

1           78. The method of claim 76, wherein said anti-mesothelin antibody is a  
2 single chain Fv antibody comprising a variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>)  
3 region.

1           79. The method of claim 78, wherein said V<sub>H</sub> region is peptide bonded to  
2 said V<sub>L</sub> region through a linker peptide.

1           80. The method of claim 78, wherein the variable heavy (V<sub>H</sub>) region is  
2 encoded by SEQ ID NO:1.

1           81. The method of claim 78, wherein the variable light (V<sub>L</sub>) region is  
2 encoded by SEQ ID NO:1.

1           82. The method of claim 78, wherein said scFv fragment comprises a  
2 variable heavy (V<sub>H</sub>) region and a variable light (V<sub>L</sub>) region of SEQ ID NO:1.

1           83. The method of claim 76, wherein said toxin is a *Pseudomonas*  
2 exotoxin (PE) or a cytotoxic fragment thereof.

1           84. The method of claim 83, wherein said PE is PE38.

1           85. The method of claim 83, wherein a variable heavy region is peptide  
2 bonded to the toxin.

1           86. The method of claim 76, wherein said malignant cell is contacted *in*  
2 *vivo*.

1           87. The method of claim 76, wherein said malignant cell is selected from  
2 the group malignancies consisting of mesotheliomas, ovarian cancer, stomach cancer and  
3 squamous cell cancer.

1                   88. A method for detecting the presence of mesothelin in a biological  
2 sample, said method comprising:

3                   (i) contacting said biological sample with an anti-mesothelin  
4 antibody which binds to recombinant mesothelin with a dissociation constant of less than  $3 \times$   
5  $10^{-8}$  M and specifically binds to cells expressing mesothelin on their cell surface;  
6                   (ii) allowing said antibody to bind to mesothelin under  
7 immunologically reactive conditions, wherein detection of said bound antibody indicates the  
8 presence of said mesothelin.

1                   89. The method of claim 88, wherein said antibody comprises CDRs as  
2 indicated in SEQ ID NO:5.

1                   90. The method of claim 88, wherein said anti-mesothelin antibody is a  
2 single chain Fv antibody comprising a variable heavy ( $V_H$ ) region and a variable light ( $V_L$ )  
3 region.

1                   91. The method of claim 90, wherein said  $V_H$  region is peptide bonded to  
2 said  $V_L$  region through a linker peptide.

1                   92. The method of claim 90, wherein the variable heavy ( $V_H$ ) region is  
2 encoded by SEQ ID NO:1.

1                   93. The method of claim 90, wherein the variable light ( $V_L$ ) region is  
2 encoded by SEQ ID NO:1.

1                   94. The method of claim 90, wherein said scFv fragment comprises a  
2 variable heavy ( $V_H$ ) region and a variable light ( $V_L$ ) region of SEQ ID NO:1.

1                   95. The method of claim 88, wherein said antibody is detectably labeled.

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1                   96. The method of claim 88, wherein the method is performed *in vivo* in a  
2                   mammal.

1                   97. A pharmaceutical composition comprising the immunoconjugate of  
2                   claim 20.

1                   98. A kit for detecting mesothelin on the surface of cells, said kit  
2                   comprising:

3                   (i) an anti-mesothelin antibody which binds to recombinant  
4                   mesothelin with a dissociation constant of less than  $3 \times 10^{-8}$  M and specifically binds to cells  
5                   expressing mesothelin on their cell surface; and  
6                   (ii) instructions printed on a tangible medium, said instructions  
7                   describing the methods of using and uses for said antibody.

Sub  
B1

ADD  
B2  
ADD  
B3  
ADD  
C1  
add 1  
C3